

**ENERGETICS IN  
BIOCHEMICAL REACTIONS**

***IRVING M. KLOTZ***

# Some Principles of ENERGETICS IN BIOCHEMICAL REACTIONS

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## Preface

With the increasing tendency to interpret biological phenomena in molecular terms, many biologists have become anxious to understand the principles of energetics which govern biochemical changes. Nevertheless, they have been understandably reluctant to devote the large amount of time that would be required even to peruse only a standard textbook in this field and to acquire the mathematical background upon which the logical development in such texts is based. However, for many purposes a "reading knowledge" of the language of thermodynamics may suffice, and this can be acquired without a large expenditure of time. With such knowledge one can at least understand the acknowledged classics in the field; some readers may even be stimulated to acquire the background to apply the concepts of energetics to branches of biology hitherto uninfluenced by these ideas.

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*Woods Hole, Massachusetts*

IRVING M. KLOTZ

## Contents

Preface	
Introduction: The Scope of Energetics	1
I. The Concept of Energy: The First Law of Thermodynamics	3
II. The Concept of Entropy: The Second Law of Thermodynamics	10
III. The Free Energy or Chemical Potential: A Criterion of Feasibility of a Material Transformation	16
IV. The Dependence of Chemical Potential on Concentration	21
V. Group Transfer Potential: "High-Energy Bond"	27
VI. Some Laws of Physicochemical Behavior	34
VII. Energetics from a Molecular-Statistical Viewpoint	44
Conclusion	64

## Introduction: The Scope of Energetics

The objective of the field of energetics or thermodynamics is to establish the principles and laws which govern material transformations. Historically speaking the subject was initially developed with a primary focus on the energy transformations which accompany these material changes; hence the name *thermodynamics* was eminently descriptive of this branch of learning. Starting near the end of the nineteenth century, however, the dominant point of view changed to one which emphasized the development and use of energy functions to describe the state of a material system and to prescribe rules which govern transitions from one state to another. The energy functions are thus used as a method of bookkeeping in correlating the behavior of matter; hence the name *energetics* is perhaps more appropriate than *thermodynamics* to describe this field of knowledge.

There have been two general approaches to the field of energetics. The classical or phenomenological one is based on purely macroscopic observations and concepts; its fundamental ideas although often highly abstract can be reduced to common experience. The statistical-molecular approach, in contrast, assumes in addition that matter consists of discrete particles, molecules, whose behavior follows the laws of mechanics. By appealing to molecular images, the statistical viewpoint provides a more concrete mechanical interpretation for thermodynamic concepts. Being based on a molecular model, statistical thermodynamics can use experimental data to provide information on molecular properties. On the other hand, the classical theory in itself is unable to give any information on molecular characteristics. However, this limitation is in a sense

also a virtue, for classical energetics is completely independent of any future changes in our conception of molecules. At least for macroscopic phenomena, classical energetics provides a completed logical framework.

We shall examine the subject of energetics first primarily from the phenomenological viewpoint since this approach requires a less sophisticated mathematical background. Once having grasped the basic principles and techniques, we shall also consider briefly some of the insights which are provided by statistical thermodynamics.

## The Concept of Energy: The First Law of Thermodynamics

Historically, the concept of energy first arose in considerations of purely mechanical phenomena. It was recognized early in mechanics that if work were done to lift a weight from one position in the gravitational field to another (Fig. I.1), this work could then be fully recovered.<sup>1</sup> Thus for example, the weight resting on the table top in Fig. I.1, if suitably connected to the weight on the floor at the right-hand side, could lift the latter to the top of the table.<sup>1</sup> Thus one may assign to the first weight on the table-top a certain "capacity to do work," which is latent in the weight by virtue of its position in the gravitational field. This capacity to do work, in the ideal situation of no friction, has the very special attribute of depending only on the height of the weight above the floor and not on the path taken to bring the weight from the floor to the table-top. It seems appropriate therefore to assign a special name, *energy*, to this capacity to do work, and perhaps to add the adjective *potential* to the word *energy* to emphasize the latent character of the work capacity in this particular example.

Work expended in causing extension of a spring is also an early example of energy in the mechanical sense. If  $x$  (Fig. I.2) represents the extension of a spring at rest, then a certain quantity of work must be exerted upon the spring to increase its extension to  $x'$ . Again this work may be recovered (fully in ideal circumstances), for

<sup>1</sup> This statement is true strictly only for the limiting case in which there is no friction at any of the mechanical contacts, e.g. between the wheel and its bearing in Fig. I.1. Likewise, it is to be understood that the weight on the left in the figure is a fraction of a milligram heavier than that on the right.



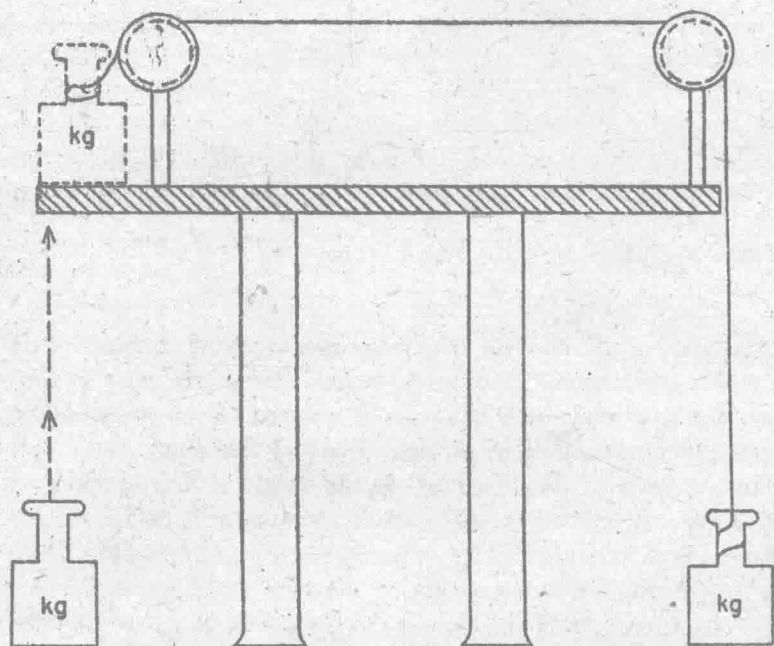


FIG. I.1.

example by attaching the extended spring to a rope and pulley system such as is shown in Fig. I.1 and raising the weight on the right side. Again the capacity of the ideal spring to do work depends only on the distance of extension  $x'$ , and hence we again may assign the special name *energy* to this capacity to do work.

One might be tempted to generalize from these two examples and think that in all cases where one exerts a force and does some work on a body, the body in its new position retains its capacity to do work. A very familiar example would immediately convince us that this generalization cannot be maintained. In Fig. I.1, for example, a substantial amount of work would be required to move the weight along the floor (particularly if the floor were very rough) from the left side to the right side of the table. In this case the weight on the right does not retain the capacity to do work. In fact one

must do work on it to return the weight to its initial position. Clearly in this situation the exertion of work on a body does not result in "giving it energy."

Paralleling historical development, ultimately we recognize an important distinction between our first two experiments and the third. In the last one, where friction is dominant, heat is evolved as the weight is moved along the floor. Since no student approaches this subject without some background in physics, he will at this point immediately say that we could call heat a form of energy. We should recognize first, however, that in doing so we have definitely

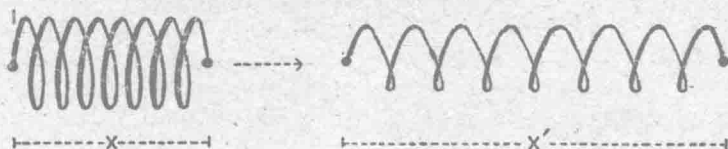


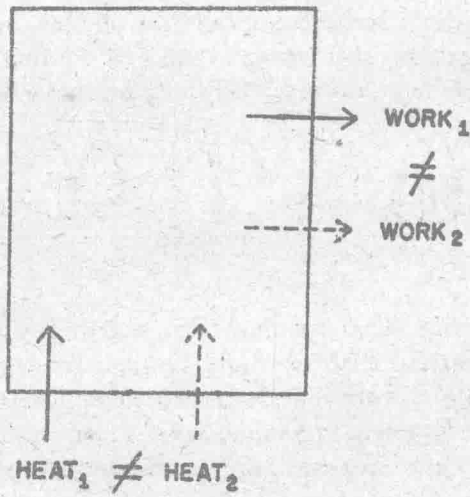
FIG. I.2.

departed from our initial definition that energy is the capacity to do work. Furthermore, there would be no advantage in making heat comparable to work unless the two were quantitatively inter-related. As every student knows, however, this quantitative equivalence has been demonstrated in the experiments of Joule.

Nevertheless, let us adopt a somewhat more sophisticated view and undertake a more general analysis of the relationships between work, heat, and energy. For this purpose we may represent merely schematically (Fig. I.3) any one of the many physical or chemical systems with which we shall be concerned. In the special circumstance illustrated, it is assumed that the system does work on the outside, but absorbs heat from the surroundings; alternative circumstances would be represented with arrows pointing in the reverse direction.

As one example of the system represented by Fig. I.3, let us consider a heavy boulder resting on the edge of a steep cliff. This boulder could be brought to the floor of the valley in many ways. One method would be to attach it to one end of a rope, attach

another boulder of almost equal weight, resting at the bottom of the valley, to the other end of the rope and by stringing the rope over a pulley wheel suitably mounted at the brink of the cliff, to allow the high boulder to be lowered to the ground while the second boulder is raised to the top of the cliff. In this procedure the first boulder does a positive amount of work, but no heat is absorbed



Nevertheless:

$$HEAT_1 - WORK_1 = HEAT_2 - WORK_2$$

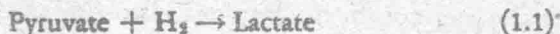
FIG. 1.3.

or evolved in the process. Another method for getting the boulder down might be to let it slide down some pathway to the valley. Less work could be obtained by this method, but a definite quantity of heat would be evolved. Many other paths could be chosen differing in the frictional resistance they would offer to the motion of the boulder. For each path the work ( $W$ ) done may differ from that for any other path, and the heat ( $Q$ ) evolved will be different. Nevertheless, despite great variations in comparative values of  $Q$  and of  $W$ ,

the difference  $Q - W$ , has been found in all experience to be the same, so long as the respective starting points and final points of the boulder's travel are the same for each path.

As another example of Fig. I.3, we might consider a stretched rubber band. The band could be attached to a weight, so that as the band contracts it does some work,  $W_1$ . In this process, a certain amount of heat,  $Q_1$ , would be absorbed. A second "path" for the return of the stretched rubber band to a shorter length might be to just let it snap back, i.e., to let  $W_2 = 0$ ; in this process, there would be an associated heat effect  $Q_2$ , different from  $Q_1$ . Once again, though, despite the inequality of  $W_1$  and  $W_2$  or  $Q_1$  and  $Q_2$ , the difference  $Q_1 - W_1$  has been found equal to  $Q_2 - W_2$ , for a wide variety of different-paths, between the same end points.

This special character of the difference  $Q - W$  is not limited to mechanical processes. Consider, for example, the chemical reaction



This reaction can take place in a suitable electrochemical cell so that electrical work is obtained as the reaction proceeds. Under certain ideal conditions the work obtained<sup>2</sup> is 11,440 calories; in this process -10,200 calories of heat are absorbed (i.e., +10,200 calories of heat are evolved by the chemicals). In contrast, the same chemical reaction can be carried out in a closed vessel without any work being obtained; under these circumstances -21,640 calories of heat are absorbed (i.e., +21,640 calories are evolved). If, following the usual convention, we call  $Q$  the heat *absorbed* by the chemical system under consideration and  $W$  the work *done* by the system, then we see once again that  $Q - W$  is the same for both methods, or paths, for carrying out the chemical reaction shown in equation (1.1).

We have considered three special cases of the schematic diagram of Fig. I.3. Going much further, we can summarize a vast amount of experience by generalizing the statements we have made for

<sup>2</sup> E. S. G. Barron and A. B. Hastings, *J. Biol. Chem.*, 107, 567 (1934).

$Q$ ,  $W$ , and  $Q - W$  so far only in our three special examples. In any system we find that although the value of  $W$ , the work done by the system, or  $Q$ , the heat absorbed by the system, in going from one state to another, varies with the path chosen, the difference  $Q - W$  is invariant and depends only on where we start and where we end. This remarkable characteristic of the difference quantity  $Q - W$  may be emphasized by giving it a special name—the change in energy,<sup>3</sup>  $\Delta E$ , of the system. In terms of a simple equation we may write

$$\Delta E = Q - W \quad (1.2)$$

The essence of the first law represented by equation (1.2) thus may be summarized in two statements. The first defines a new concept, energy, in terms of directly measurable concepts, heat and work. The second declares that the internal energy, so defined, is a thermodynamic property; that is, it depends only on the state of a system and not on the previous history of the system. To repeat, despite the fact that the heat absorbed,  $Q$ , and the work done,  $W$ , in going from one state to another depend on the particular path used in the transformation, the difference in the two quantities, defined as  $\Delta E$ , is independent of the method by which the change is accomplished.

It is, furthermore, a necessary consequence of these statements that  $\Delta E$  around a closed path is zero. If the system is ultimately returned to its initial state, there can be no change in its energy, since  $E$  depends only on the state of the system, which has not changed in a cyclic process. Despite this fact, the total  $Q$  or  $W$  for the cyclical process may differ very much from zero.

It should also be noticed that the very definition of the energy concept precludes the possibility of determining absolute values; that is, we have defined only a method of measuring *changes* in

<sup>3</sup> We shall use the symbol  $E$  for the internal energy of a system. The first law of thermodynamics permits us to define, however, only changes in energy,  $E_2 - E_1$ , where  $E_2$  is the energy of the system at the end of a process and  $E_1$  that at the beginning. For  $E_2 - E_1$  we shall use the briefer notation  $\Delta E$ .

internal energy in terms of heat and work quantities. Classical energetics, by itself, is incapable of determining the absolute zero of reference for the energy function. In practice this limitation is not really a handicap, however, since interest is generally focused on chemical and physical *transformations*, and any convenient state may be chosen as the reference point.

## II

### The Concept of Entropy: The Second Law of Thermodynamics

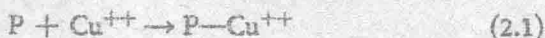
We shall be interested in the principles of energetics primarily for their ability to tell us whether a particular biochemical (or biophysical) change is feasible under a specified set of conditions. The first law of thermodynamics, however, does not provide us with a criterion for determining when a transformation may occur spontaneously, as a few specific examples will show.

One unfamiliar with energetics is accustomed to think that a chemical or physical change may occur spontaneously only if the final state of the system is at a lower level of energy than the initial (i.e., if  $\Delta E$  is  $-$ ). This conclusion is based on thoroughly valid common experience with movements in gravitational fields. We all recognize that a ball tends to fall from a higher to a lower level, not vice versa. For purely mechanical processes, involving no heat exchange, the rule that  $\Delta E$  must be negative is valid as a criterion of permissible spontaneous change. What is not often realized is that this rule is completely unreliable if applied to all kinds of transformations.

There are spontaneous transformations which occur despite the fact that the internal energy of the system at the end is essentially the same as before the transformation. For example, when a stretched rubber band is released, it snaps back spontaneously; yet  $\Delta E$  for this process is substantially zero.

There are even processes which can occur spontaneously despite the fact that the internal energy at the end is greater than at the

beginning of the transformation (i.e., for which  $\Delta E$  is  $+$ ). These are particularly common among chemical changes. For example, when a free copper ion and a protein molecule (P) are permitted to come in contact with each other, they will spontaneously form a complex compound:



Nevertheless for this reaction  $\Delta E$  is  $+3$  kcal.; that is,  $P\text{---Cu}^{++}$  has 3 kcal. more internal energy than separated P and  $\text{Cu}^{++}$  particles.

Thus reactions may occur spontaneously for which  $\Delta E$  is  $-$ , 0 or  $+$  (Fig. II.1). Clearly  $\Delta E$  is no criterion of permissibility of a transformation. Apparently the first law of thermodynamics does not contain within it the basis of any criterion of spontaneity. Some further principle will be required to summarize in a general statement the observed tendency of systems of many different types to change in a particular direction.

Let us examine again a process of the type shown in Fig. II.1 (C), that is, one which proceeds spontaneously to a state of higher energy. At first glance the occurrence of this transformation might seem to violate the first law, for how can a system spontaneously acquire energy? Actually, of course, this system does not violate the first law; during the spontaneous transformation it absorbs heat [3 kcal. in Fig. II.1 (C)] spontaneously.

Evidently, then, some chemical systems are capable of spontaneously absorbing heat from their surroundings in order to proceed to a higher energy state, whereas others are not. Is there any way of telling which systems will behave in each way?

Since  $\Delta E$  as a criterion of spontaneity fails for transformations involving heat exchange, we might expect a successful, generally applicable criterion to involve  $Q$  in some fashion. Clearly the proper criterion does not depend directly on  $Q$ , since reactions proceed spontaneously for which  $Q$  is positive, negative or zero. It would seem reasonable, however, if a suitable rule were developed containing some modified function of  $Q$ .



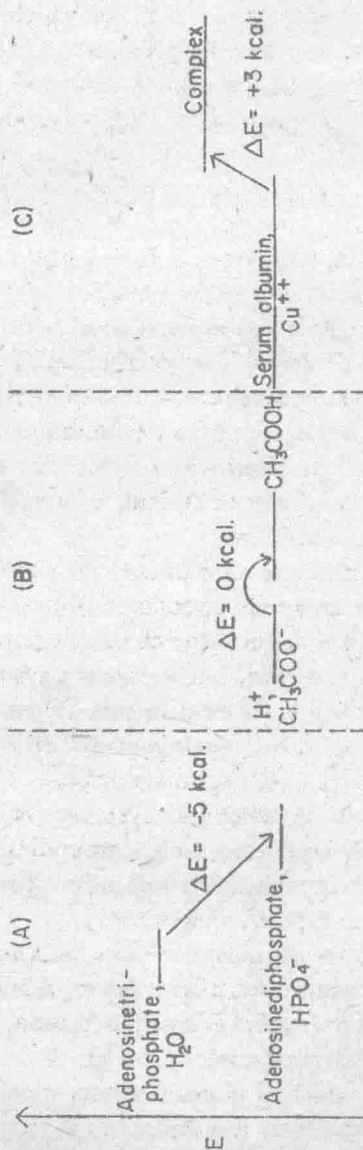


FIG. II.1. Change in energy for some chemical transformations all occurring spontaneously.